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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/511,155	10/14/2004	Oliver Schadt	MERCK-2932	9151

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EXAMINER	
SHIAO, REI TSANG	
ART UNIT	**PAPER NUMBER**
1626	

MAIL DATE	DELIVERY MODE
03/17/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/511,155	SCHADT ET AL.	
	Examiner	Art Unit	
	Rei-tsang Shiao, Ph.D.	1626	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *11 December 2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-7,9,10,12-16 and 18-22* is/are pending in the application.

4a) Of the above claim(s) *18 and 19* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-7, 9-10, 12-16 and 20-22* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

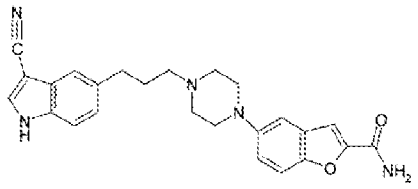
DETAILED ACTION

1. This application claims benefit of the foreign application:

GERMANY 10217006.1 with a filing date 04/16/2002.

2. Amendment of claims 1-3, 5, 13 and 18-22, cancellation of claims 8, 11, and 17, and Fiebig et al. publication in EXHIBIT A in the amendment filed on December 11, 2007 is acknowledged. Claims 1-7, 9-10, 12-16 and 18-22 are pending in the application.

Responses to Election/Restriction

3. Applicant's election with traverse of election of Group I claims 1-7, 9-10, 12-16 and 20-22, in part, in the reply filed on July 20, 2007 is acknowledged. Election of a single disclosed species, i.e.,  , is also acknowledged.

Claims 1-7, 9-10, 12-16 and 18-22 are pending in the application. The scope of the invention of the elected subject matter is as follows.

Claims 1-7, 9-10, 12-16 and 20-22, in part, drawn to compounds/compositions of formula (I), wherein the variable R^2- R^5 independently does not contain a Het moiety (i.e., heterocyclic radical) thereof, the variables R^2- R^5 independently is not substituted with a Het moiety (i.e., heterocyclic radical) thereof, the variables E and G together with the N atom to which they are bonded, are piperazine or piperidine thereof, when the variable Z represents an aromatic carbocyclic radical or heterocyclic radical and the heterocyclic radical is selected from the group consisting of thiophene, pyrrolyl,

pyrazole, benzopyrane, benzofurane, benzodioxine, thiazole, benzothiadiazole, benzothiazole, pyridine, pyrimidine, indole, triazole, and quinoline thereof, their processes of making and methods of use (i.e., treating depression).

The claims 1-7, 9-10, 12-16 and 18-22 herein lack unity of invention under PCT rule 13.1 and 13.2 since the compounds defined in the claims lack a significant structural element qualifying as the special technical feature that defines a contribution over the prior art, see Halazy et al. US 5,726,177. Chakravarty et al. disclose similar piperazine/indole compounds as the instant invention. Accordingly, unity of invention is considered to be lacking and restriction of the invention in accordance with the rules of unity of invention is considered to be proper. Furthermore, even if unity of invention under 37 CFR 1.475(a) is not lacking, which it is lacking, under 37 CFR 1.475(b) a national stage application containing claims to different categories of invention will be considered to have unity of invention if the claims are drawn only to one of the following combinations:

(1) A product and a process specially adapted for the manufacture of said product', or

(2) A product and a process of use of said product; or

(3) A product, a process specially adapted for the manufacture of the said product, and a use of the said product; or

(4) A process and an apparatus or means specifically designed for carrying out the said process; or

(5) A product, a process specially adapted for the manufacture of the said product, and an apparatus or means specifically designed for carrying out the said process.

And, according to 37 CFR 1.475(c)

if an application contains claims to more or less than one of the combinations of categories of invention set forth in paragraph (b), unity of invention might not be present.

However, it is noted that unity of invention is considered lacking under 37 CFR 1.475(a) and (b). Therefore, since the claims are drawn to more than a product, and according to 37 CFR 1.475 (e)

> the determination whether a group of inventions is so linked as to form a single general inventive concept shall be made without regard to whether the inventions are claimed in separate claims or as alternatives within a single claim.

The claims lack unity of invention and should be limited to only a product, or a process for the preparation, or a use of the said product. In the instant case, Groups I-IV are drawn to various products of formula (I)-(III), and the final products do not contain a common technical feature or structure, and do not define a contribution over the prior art, i.e., similar piperazine/indole compounds. Moreover, compounds of formulae (II)-(III) of claims 18-19 are drawn to starting materials for preparing compounds of formula (I), which are distinct invention from claims 1-7, 9-10, 12-16 and 20-22. Moreover, the examiner must perform a commercial database search on the subject matter of each group, especially an additional search for claims 18-19, in addition to a paper search, which is quite burdensome to the examiner.

Claims 1-7, 9-10, 12-16 and 20-22, in part, embraced in above elected subject matter, are prosecuted in the case. Claims 1-7, 9-10, 12-16 and 20-22, in part, not embraced in above elected subject matter, and claims 18-19 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention.

The requirement is still deemed proper and therefore is made FINAL.

Responses to Amendment/Arguments

4. Applicant's arguments regarding the rejection of claims 9-10 and 12-16 under 35 U.S.C. 112, first paragraph filed on December 11, 2007 have been fully considered but they are not persuasive. A number of case laws have been cited by applicants, i.e., *In Cross v. Lizuka*, 224 USPQ 739 (Fed. Cir. 1985) and *Fujikawa v. Watanasin*, 39 USPQ.2d 1895 (1966). It is noted that the level of the skill in the chemical arts is high, it would require undue experimentation of one of ordinary skill in the art to resolve There are no *in vitro* working examples present directly for the treatment of any cells which the activity of an excitatory amino acid in a cell is inhibited by the administration of the instant invention. There are no direct *in vivo* (i.e., animal model) evidence or working examples wherein any diseases or conditions is treated using the instant compounds of formula (I). Furthermore, the instant claims cover "inhibiting an excitatory amino acid in a cell" that are known to exist and those that may be discovered in the future, for which there is no enablement provided. additionally, there is no reasonable basis for assuming the instant compounds of formula (I) embraced by the claims will share the same physiological properties. The methods of use (i.e., 5HT reuptake-inhibiting and 5HTx-agonistic and/or -antagonistic actions and treating schizophrenia) disclosed in the embodiment in page 5, lines 20-24 and page 6, lines 15-25 are not supported by any biological assays *in vitro* or *in vivo* using the instant compounds of formula (I). The specification lacks evidence of reduction of practice for the instant invention.

Genentech Inc. v. Novo Nordisk A/S (CA FC) 42 USPQ2d 1001, states that " a

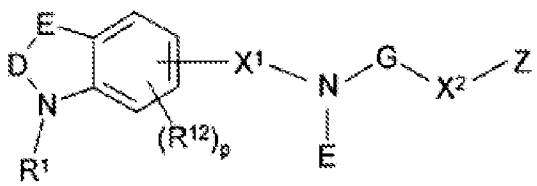
patent is not a hunting license. It is not a reward for search, but compensation for its successful conclusion" and "patent protection is granted in return for an enabling disclosure of an invention, not for vague intimations of general ideas that may or may not be workable".

Fiebig et al. publication does not disclose the instant methods of use using the instant compounds of formula (I), especially the disclosure of correlation of *in vitro* to *in vivo* activity as a basis for anticancer does not provide enablement for the instant invention. The rejection of claims 9-10 and 12-16 under 35 U.S.C. 112, first paragraph is maintained.

5. Since the instant variable X1 of formula (I) does not represents (CHR^7)h-Q-(CHR^8)k, therefore the rejection of 1-3, 5-7, 12-16 and 20-22 under 35 U.S.C. 102(a) or 102 (b) over Halazy et al. '177, Bottcher et al. '461 or Bottcher et al. '725 has been overcome in the amendment filed on December 11, 2007.

6. Applicant's arguments regarding the rejection of claims 1-7, 9-10, 12-16 and 20-22 under 35 U.S.C. 103(a) over Halazy et al. US 5,726,177 filed on December 11, 2007 have been fully considered but they are not persuasive.

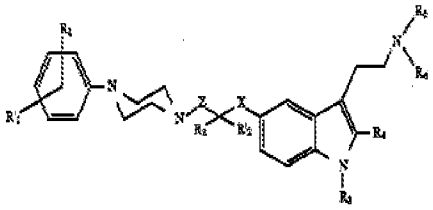
Applicants claims piperazine compound/compositions of formula (I), i.e.,



, wherein the variables E and G together with the N atom to which they are bonded, are piperazine or piperidine

thereof; the variable X2 represents a bond, the variable Z represents aromatic carbocyclic radical (i.e. phenyl) substituted with the variables R2 to R5, and the variables R2 to R5 independently represent (CH_2)nCN or (CH_2)nNR^6COR^6, and the variable n is 0, the variable R^6 represents the variable A and the variable A represents alkyl; the variable D-E represents $R^2C=CR^4$ and the variable R^2 or R^4 independently represents (CH_2)n$N(R^6)_2$ and the variable R^6 represents the variable A and the variable A represents alkyl or hydrogen, see claim 1.

Halazy et al. disclose piperazine compound/composition of formula (I), i.e.,



, the variable Z rrepresents (CH2)n and the variable n is 1; or C=S, the variable X represents CH2, the variable R_1 or $R_{1'}$ independently represents hydrogen, CN, $NHCOR_7$ or $NHCONR_5R_7$ and the variable R_5 or R_7 independently represents hydrogen or alkyl, see columns 2-3.

The difference between the instant claims and Halazy et al. is that the variables E and G together with the N atom to which they are bonded, are piperazine or piperidine thereof, while Halazy et al. represents piperazine at the same position. Halazy et al. compounds/compositions overlap with the instant invention.

One having ordinary skill in the art would find the instant claims 1-7, 9-10, 12-16 and 20-22 prima facie obvious **because** one would be motivated to employ the analogue compounds/compositions of Halazy et al. to obtain the instant

compounds/composition of formula (I), wherein the variables E and G together with the N atom to which they are bonded, are piperazine thereof; the variable X2 represents a bond, the variable Z represents aromatic carbocyclic radical (i.e. phenyl) substituted with the variables R2 to R5, and the variables R2 to R5 independently represent (CH_2)nCN or (CH_2)nNR^6COR^6, and the variable n is 0, the variable R^6 represents the variable A and the variable A represents alkyl; the variable D-E represents $R^2C=CR^4$ and the variable R^2 or R^4 independently represents (CH_2)n$N(R^6)_2$ and the variable R^6 represents the variable A and the variable A represents alkyl or hydrogen.

The motivation to obtain the claimed compounds/compositions derives from known Halazy et al. compounds would possess similar activities (i.e., agents for pharmaceuticals) to that which is claimed in the reference. The rejection of claims 1-7, 9-10,12-16 and 20-22 under 35 U.S.C. 103(a) over Halazy et al. US 5,726,177 is maintained.

7. Since the instant variable X1 of formula (I) does not represents (CHR7)h-Q-(CHR8)k1, therefore the rejection of claims 1-7, 9-10, 12-16 and 20-22 under 35 U.S.C. 103(a) over Bottcher et al. US 6,838,461 or US 6,723,725 has been overcome in the amendment filed on December 11, 2007.

8. Since the instant variable X1 of formula (I) does not represents (CHR7)h-Q-(CHR8)k1, therefore the rejection of claims 1-7, 9-10, 12-16 and 20-22 under the obviousness-type double patenting over Bottcher et al. US 6,838,461 or over US 6,723,725 has been overcome in the amendment filed on December 11, 2007.

Claim Objections

9. Claims 1-7, 9-10, 12-16 and 20-22 are objected to as containing non-elected subject matter, i.e., Het, benzo[d]isothiazole, imidazole, pyrrolidine of claim 4, etc. It is suggested that applicants amend the claims to the scope of the elected subject matter as defined on the paragraph 3 *supra*.

10. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Rei-tsang Shiao whose telephone number is (571) 272-0707. The examiner can normally be reached on 8:30 AM - 5:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Joseph K. McKane can be reached on (571) 272-0699. The fax phone

number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/REI-TSANG SHIAO /

Rei-tsang Shiao, Ph.D.
Primary Patent Examiner
Art Unit 1626

March 07, 2008